

Amendment to the Claims:

Please cancel claims 6, 7, 81, 82 and 88, without prejudice

Please amend the claims as follows:

This listing of claims will replace all prior versions, and listing, of claims in the application:

Listing of Claims:

Claim 1 (original): A method of screening for an antimicrobial agent, comprising the steps of:

(a) providing a test compound, a microbial proliferation gene and a first and a second sample of a microorganism,

wherein the microbial proliferation gene is identified by introducing an exogenous nucleic acid into the microorganism, the exogenous nucleic acid having substantial sequence identity to an endogenous microbial gene, wherein the exogenous nucleic acid is a random fragment or a random sequence, and, identifying the endogenous gene as a microbial proliferation gene by comparing the proliferation or viability of the microorganism when the exogenous nucleic acid is expressed in or introduced into the microorganism with the proliferation or viability of the microorganism when the exogenous nucleic acid is not present or not expressed,

(b) introducing the microbial proliferation gene into the microorganism of the first sample;

(c) contacting the test compound with the first sample and the second microorganism samples; and

(d) determining the effect of the test compound on the first and the second microorganism samples, wherein the test compound is identified as an antimicrobial agent by comparing the effect of contacting the test compound to the first sample, where the exogenous nucleic acid is expressed or introduced, to the effect of contacting the test compound to the second sample, where the exogenous nucleic acid is not present, and the effect of the test compound on the contacted microorganism differs between the first and the second samples, thereby identifying the test compound as an antimicrobial agent.

Claim 2 (original): The method of claim 1, wherein the effect of contacting the test compound with the microorganism is a change in the rate of proliferation of the contacted first microorganism sample as compared to the contacted second microorganism sample, thereby identifying the test compound as an anti-proliferative antimicrobial agent.

Claim 3 (original): The method of claim 1, wherein the effect of contacting the test compound with the microorganism is a microbiostatic effect on the contacted first microorganism sample as compared to the contacted second microorganism sample, thereby identifying the test compound as a microbiostatic antimicrobial agent.

Claim 4 (original): The method of claim 1, wherein the effect of contacting the test compound with the microorganism is a microbiocidal effect on the contacted first microorganism as compared to the contacted second microorganism sample, thereby identifying the test compound as a microbiocidal antimicrobial agent.

Claim 5 (original): The method of claim 1, wherein the effect of contacting the test compound with the first microorganism sample as compared to the second microorganism sample is a change in the rate of transcription or amount of a transcription product of the microbial proliferation gene in the first microorganism sample.

Claims 6 and 7 (canceled)

Claim 8 (original): The method of claim 1, wherein the effect of contacting the antimicrobial agent with the microorganism is a change in the rate of translation or amount of a translation product of the microbial proliferation gene.

Claim 9 (original): The method of claim 8, wherein the translation product is a polypeptide.

Claim 10 (original): The method of claim 1, wherein the effect of contacting the test compound with the microorganism is a change in the activity of a translation product of the microbial proliferation gene.

Claim 11 (original): The method of claim 1, wherein the effect of contacting the test compound with the microorganism is a change in metabolism of the contacted microorganism.

Claim 12 (original): The method of claim 1, wherein the effect of contacting the test compound with the microorganism is a change in viability of the contacted microorganism.

Claim 13 (original): The method of claim 1, wherein an effect of the test compound is determined indirectly.

Claim 14 (original): The method of claim 13, wherein an effect of the test compound is determined by a protein activity assay.

Claim 15 (original): The method of claim 14, wherein the effect of the test compound agent is determined by an enzyme assay.

Claim 16 (original): The method of claim 13, wherein the effect of the test compound is determined by an immunoassay.

Claim 17 (original): The method of claim 1, wherein the effect of contacting the test compound with the microorganism is a change in the rate of proliferation, metabolism or viability of the contacted first microorganism sample as compared to the contacted second microorganism sample, thereby identifying the test compound as an antibiotic.

Claim 18 (original): The method of claim 1, wherein introducing the microbial proliferation gene into the microorganism of the first sample results in an increased level of

expression of the transcription or translation product of the gene, thereby requiring contacting more test compound to the first sample than to the second sample to have the same effect on the microorganism.

Claim 19 (original): The method of claim 1, wherein introducing the microbial proliferation gene into the microorganism of the first sample results in an decreased level of expression or activity of the translation product of an endogenous microbial proliferation gene, thereby requiring contacting less test compound to the first sample than to the second sample to have the same effect on the microorganism.

Claim 20 (original): The method of claim 19, wherein the microbial proliferation gene is operably linked to a transcriptional regulatory element effective for controlling expression of the exogenous nucleic acid.

Claim 21 (original): The method of claim 20, wherein the transcriptional regulatory element effective for controlling expression of the microbial proliferation gene is an inducible regulatory sequence.

Claim 22 (original): The method of claim 21, wherein the inducible regulatory sequence that controls expression of the microbial proliferation gene is a promoter induced in response to a chemical inducer.

Claim 23 (original): The method of claim 22, wherein chemical inducer comprises isopropyl-beta-D-thiogalactopyranoside, tetracycline or tryptophan.

Claim 24 (original): The method of claim 21, wherein the inducible regulatory sequence that controls expression of the microbial proliferation gene is a promoter induced in response to environmental changes.

Claim 25 (original): The method of claim 20, wherein the microbial proliferation gene is operably linked in an antisense orientation to the transcriptional regulatory element.

Claim 26 (original): The method of claim 20, wherein the microbial proliferation gene is operably linked in a sense orientation to the transcriptional regulatory element.

Claim 27 (original): The method of claim 1, wherein introducing the microbial proliferation gene into the microorganism of the first sample results in an decreased level of expression of the transcription product of an endogenous microbial proliferation gene, thereby requiring contacting less test compound to the first sample than to the second sample to have the same effect on the microorganism.

Claim 28 (original): The method of claim 27, wherein the microbial proliferation gene is operably linked to a transcriptional regulatory element effective for controlling expression of the exogenous nucleic acid.

Claim 29 (original): The method of claim 28, wherein the transcriptional regulatory element effective for controlling expression of the microbial proliferation gene is an inducible regulatory sequence.

Claim 30 (original): The method of claim 29, wherein the inducible regulatory sequence that controls expression of the microbial proliferation gene is a promoter induced in response to a chemical inducer.

Claim 31 (original): The method of claim 30, wherein chemical inducer comprises isopropyl-beta-D-thiogalactopyranoside, tetracycline or tryptophan.

Claim 32 (original): The method of claim 29, wherein the inducible regulatory sequence that controls expression of the microbial proliferation gene is a promoter induced in response to environmental changes.

Claim 33 (original): The method of claim 28, wherein the microbial proliferation gene is operably linked in an antisense orientation to the transcriptional regulatory element.

Claim 34 (original): The method of claim 28, wherein the microbial proliferation gene is operably linked in a sense orientation to the transcriptional regulatory element.

Claim 35 (original): The method of claim 1, wherein the microbial proliferation gene is endogenous to the microorganism.

Claim 36 (original): The method of claim 1, wherein the microbial proliferation gene is a bacterial proliferation gene.

Claim 37 (original): The method of claim 36, wherein the bacterial proliferation gene has substantial sequence identity to the E. coli *viaA* gene.

Claim 38 (withdrawn): The method of claim 36, wherein the bacterial proliferation gene has substantial sequence identity to the E. coli *orf1* gene.

Claim 39 (withdrawn): The method of claim 36, wherein the bacterial proliferation gene has substantial sequence identity to the E. coli *lepB* gene.

Claim 40 (withdrawn): The method of claim 36, wherein the bacterial gene has substantial sequence identity to the E. coli *ugpB* gene.

Claim 41 (withdrawn): The method of claim 36, wherein the bacterial proliferation gene has substantial sequence identity to the E. coli *ddlB* gene.

Claim 42 (withdrawn): The method of claim 36, wherein the bacterial proliferation gene has substantial sequence identity to the E. coli *secA* gene.

Claim 43 (withdrawn): The method of claim 36, wherein the bacterial proliferation gene has substantial sequence identity to a gene having sequence identity to *E. coli* fimF or fimD.

Claim 44 (original): The method of claim 1, wherein the microorganism is a pathogen.

Claim 45 (original): The method of claim 1, wherein the microorganism is a bacterium.

Claim 46 (original): The method of claim 45, wherein the bacterium is a pathogen.

Claim 47 (original): The method of claim 45, wherein the bacterium is a gram-negative bacterium.

Claim 48 (original): The method of claim 47, wherein the gram-negative bacterium is *Escherichia coli*.

Claim 49 (original): The method of claim 47, wherein the bacterium is a gram-positive bacterium.

Claim 50 (original): The method of claim 49, wherein the gram-positive bacterium is *Staphylococcus aureus*.

Claim 51 (withdrawn): The method of claim 1, wherein the microorganism is a fungus.

Claim 52 (withdrawn): The method of claim 1, wherein the microorganism is a yeast.

Claim 53 (withdrawn): The method of claim 1, wherein the microorganism is an Archaeobacteria.

Claim 54 (original): The method of claim 44, wherein the microorganism is a human pathogen.

Claim 55 (original): The method of claim 44, wherein the microorganism is an animal pathogen.

Claim 56 (withdrawn): The method of claim 44, wherein the microorganism is a plant pathogen.

Claim 57 (original): The method of claim 1, wherein the exogenous nucleic acid is operably linked to a transcriptional regulatory element effective for controlling expression of the exogenous nucleic acid.

Claim 58 (original): The method of claim 57, wherein the transcriptional regulatory element effective for controlling expression of the exogenous nucleic acid is an inducible regulatory sequence.

Claim 59 (original): The method of claim 58, wherein the inducible regulatory sequence that controls expression of the exogenous nucleic acid is a promoter induced in response to a chemical inducer.

Claim 60 (original): The method of claim 59, wherein chemical inducer comprises isopropyl-beta-D-thiogalactopyranoside, tetracycline or tryptophan.



Claim 61 (original): The method of claim 58, wherein the inducible regulatory sequence that controls expression of the exogenous nucleic acid is a promoter induced in response to environmental changes.

Claim 62 (original): The method of claim 57, wherein the exogenous nucleic acid is operably linked in an antisense orientation to the transcriptional regulatory element.

Claim 63 (original): The method of claim 57, wherein the exogenous nucleic acid is operably linked in a sense orientation to the transcriptional regulatory element.

Claim 64 (original): The method of claim 1, wherein the exogenous nucleic acid further comprises a vector.

Claim 65 (original): The method of claim 64, wherein the vector is a plasmid or a phage vector.

Claim 66 (original): The method of claim 1, wherein the exogenous nucleic acid is from about 10 to about 5,000 nucleotides in length.

Claim 67 (original): The method of claim 66, wherein the exogenous nucleic acid is from about 15 to about 1,500 nucleotides in length.

Claim 68 (original): The method of claim 1, wherein the exogenous nucleic acid is obtained from a nucleic acid selected from the group consisting of chromosomal DNA, episomal genomic DNA, RNA, cDNA and synthetic DNA.

Claim 69 (original): The method of claim 1, wherein the test compound comprises a combinatorial library.

Claim 70 (original): The method of claim 1, wherein the test compound comprises an inorganic compound.

Claim 71 (original): The method of claim 1, wherein the test compound comprises an organic compound.

Claim 72 (original): The method of claim 1, wherein the test compound comprises a peptidomimetic.

Claim 73 (original): The method of claim 1, wherein the test compound comprises a polypeptide or a peptide.

Claim 74 (original): The method of claim 1, wherein the test compound comprises an oligonucleotide or a polynucleotide.

Claim 75 (original): The method of claim 1, wherein determining the effect of the test compound on the microorganism comprises comparative or replica plating of the microorganism.

Claim 76 (original): The method of claim 1, wherein determining the effect of the test compound on the microorganism comprises measuring respiratory activity.

Claim 77 (original): The method of claim 1, wherein determining the effect of the test compound on the microorganism comprises measuring colony-forming units, light scattering or optical density, the number of organisms in a particle counter, the fluorescence of cell cultures or of individual cells after addition of fluorescent dyes, the incorporation of precursors to macromolecules or the uptake of metabolites.

Claim 78 (original): The method of claim 1, wherein the microorganism is a viable cell.

Claim 79 (original): The method of claim 1, wherein the microorganism is a crude cell lysate.

Claim 80 (original): The method of claim 1, wherein the test compound targets a transcription product of the microbial proliferation gene.

Claims 81 and 82 (canceled)

Claim 83 (original): The method of claim 80, wherein the test compound selectively binds to the transcription product.

Claim 84 (original): The method of claim 1, wherein the test compound targets a translation product of the microbial proliferation gene.

Claim 85 (original): The method of claim 84, wherein the translation product is a polypeptide.

Claim 86 (original): The method of claim 84, wherein the test compound selectively binds to the translation product.

Claim 87 (original): A method of screening for antibacterial agents, comprising the steps of:

(a) providing a test compound, a microbial proliferation gene and a first and a second sample of a bacterium,

wherein the bacterial proliferation gene is identified by introducing an exogenous nucleic acid into the bacterium, the exogenous nucleic acid having substantial sequence identity to an endogenous bacterial gene, wherein the exogenous nucleic acid is a random fragment or a random sequence, and, identifying the endogenous gene as a bacterial proliferation gene by comparing the proliferation or viability of the bacterium when the exogenous nucleic acid is

expressed in or introduced into the bacterium with the proliferation or viability of the bacterium when the exogenous nucleic acid is not present or not expressed,

(b) introducing the bacterial proliferation gene into the bacterium of the first sample;

(c) contacting the test compound with the first sample and the second bacterium samples; and

(d) determining the effect of the test compound on the first and the second bacterial samples, wherein the test compound is identified as an anti-proliferative anti-bacterial agent by comparing the effect of contacting the test compound to the first sample, where the exogenous nucleic acid is expressed or introduced, to the effect of contacting the test compound to the second sample, where the exogenous nucleic acid is not present, and the effect of the test compound on the contacted bacterium differs between the first and the second samples, thereby identifying the test compound as an anti-bacterial agent.

Claim 88 (canceled)

Claim 89 (previously presented): A method of screening for an antimicrobial agent, comprising the steps of:

(a) providing a test compound, a microbial proliferation gene and a first and a second sample of a first microorganism,

wherein the microbial proliferation gene is identified by introducing an exogenous nucleic acid into the first microorganism and the exogenous nucleic acid has substantial sequence identity to a microbial gene endogenous to the first microorganism and is a random fragment or a random sequence and is derived from a second microorganism, and, identifying the endogenous gene as a microbial proliferation gene by comparing the proliferation or viability of the first microorganism when the exogenous nucleic acid is expressed in or introduced with the proliferation or viability of the first microorganism when the exogenous nucleic acid is not present or not expressed,

(b) introducing the microbial proliferation gene into the first microorganism of the first sample;

(c) contacting the test compound with the first sample and the second microorganism samples; and

(d) determining the effect of the test compound on the first and the second microorganism samples, wherein the test compound is identified as an antimicrobial agent by comparing the effect of contacting the test compound to the first sample, where the exogenous nucleic acid is expressed or introduced, to the effect of contacting the test compound to the second sample, where the exogenous nucleic acid is not present or is not expressed, and the effect of the test compound on the contacted microorganism differs between the first and the second samples, thereby identifying the test compound as an antimicrobial agent.

Claim 90 (previously presented): A method of screening for antibacterial agents, comprising the steps of:

(a) providing a test compound, a microbial proliferation gene and a first and a second sample of a first bacterium,

wherein the bacterial proliferation gene is identified by introducing an exogenous nucleic acid into the first bacterium and the exogenous nucleic acid has substantial sequence identity to a bacterial gene endogenous to the first bacterium and the exogenous nucleic acid is a random fragment or a random sequence and is derived from a second bacterium, and, identifying the endogenous gene as a bacterial proliferation gene by comparing the proliferation or viability of the first bacterium when the exogenous nucleic acid is expressed in or introduced with the proliferation or viability of the first bacterium when the exogenous nucleic acid is not present or not expressed,

(b) introducing the bacterial proliferation gene into the first bacterium of the first sample;

(c) contacting the test compound with the first sample and the second bacterium samples; and

(d) determining the effect of the test compound on the first and the second bacterial samples, wherein the test compound is identified as an anti-proliferative anti-bacterial agent by comparing the effect of contacting the test compound to the first sample, where the exogenous nucleic acid is expressed or introduced, to the effect of contacting the test compound

to the second sample, where the exogenous nucleic acid is not present or is not expressed, and the effect of the test compound on the contacted bacterium differs between the first and the second samples, thereby identifying the test compound as an anti-bacterial agent.

Claim 91 (previously presented): A method of screening for an antimicrobial agent, comprising the steps of:

(a) providing a test compound, a microbial gene essential for viability or growth and a first and a second sample of a microorganism,

wherein the microbial gene essential for viability or growth is identified by introducing an exogenous nucleic acid into the microorganism and the exogenous nucleic acid is a random fragment or a random sequence, and, identifying the endogenous gene as a gene essential for viability or growth by comparing the proliferation or viability of the microorganism when the exogenous nucleic acid is expressed in or introduced with the proliferation or viability of the microorganism essential for viability or growth when the exogenous nucleic acid is not present or not expressed,

(b) introducing the microbial gene into the microorganism of the first sample;

(c) contacting the test compound with the first sample and the second microorganism samples; and

(d) determining the effect of the test compound on the first and the second microorganism samples, wherein the test compound is identified as an antimicrobial agent by comparing the effect of contacting the test compound to the first sample, where the exogenous nucleic acid is expressed or introduced, to the effect of contacting the test compound to the second sample, where the exogenous nucleic acid is not present or not expressed, and the effect of the test compound on the contacted microorganism differs between the first and the second samples, thereby identifying the test compound as an antimicrobial agent.

Claim 92 (previously presented): A method of screening for an anti-bacterial agent, comprising the steps of:

(a) providing a test compound, a gene essential for viability or growth and a first and a second sample of a bacterium,

wherein the gene essential for viability or growth is identified by introducing an exogenous nucleic acid into the bacterium and the exogenous nucleic acid is a random fragment or a random sequence, and, identifying the endogenous gene essential for viability or growth by comparing the proliferation or viability of the bacterium when the exogenous nucleic acid is expressed in or introduced with the proliferation or viability of the bacterium when the exogenous nucleic acid is not present or not expressed,

(b) introducing the exogenous gene into the bacterium of the first sample;

(c) contacting the test compound with the first sample and the second bacterial samples; and

(d) determining the effect of the test compound on the first and the second bacterial samples, wherein the test compound is identified as an anti-bacterial agent by comparing the effect of contacting the test compound to the first sample, where the exogenous nucleic acid is expressed or introduced, to the effect of contacting the test compound to the second sample, where the exogenous nucleic acid is not present or not expressed, and the effect of the test compound on the contacted bacterium differs between the first and the second samples, thereby identifying the test compound as an anti-bacterial agent.

Claim 93 (previously presented): A method of screening for an antimicrobial agent, comprising the steps of:

(a) providing a test compound, a microbial proliferation gene and a first and a second sample of a first microorganism,

wherein the microbial proliferation gene is identified by introducing an exogenous nucleic acid into the first microorganism and the exogenous nucleic acid has substantial sequence identity to a microbial gene endogenous to the first microorganism and is a random antisense fragment or a random antisense sequence, and, identifying the endogenous gene as a microbial proliferation gene by comparing the proliferation or viability of the first microorganism when the exogenous nucleic acid is expressed in or introduced with the proliferation or viability of the first microorganism or an equivalent microorganism when the exogenous nucleic acid is not present or not expressed,

(b) introducing the microbial proliferation gene into the first microorganism of the first sample;

(c) contacting the test compound with the first sample and the second microorganism samples; and

(d) determining the effect of the test compound on the first and the second microorganism samples, wherein the test compound is identified as an antimicrobial agent by comparing the effect of contacting the test compound to the first sample, where the exogenous nucleic acid is expressed or introduced, to the effect of contacting the test compound to the second sample, where the exogenous nucleic acid is not present or is not expressed, and the effect of the test compound on the contacted microorganism differs between the first and the second samples, thereby identifying the test compound as an antimicrobial agent.